Supplement Article

Psychiatric Barriers to Readiness for Treatment for Hepatitis C Virus (HCV) Infection among Injection Drug Users: Clinical Experience of an Addiction Psychiatrist in the HIV-HCV Coinfection Clinic of a Public Health Hospital

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Among injection drug users, psychological and psychiatric barriers to readiness for treatment for hepatitis C virus (HCV) infection include mood and anxiety disorders, cognitive deficits, temperament disorders, and personality vulnerabilities, as well as ongoing drug use. Many aspects of these barriers can be overcome with direct treatment or social support. To establish effective treatment for HCV infection in this population of patients, it is essential that the patient and providers develop a rapport that allows for active communication. It is also important that the patient make an effort to adhere to the treatment requirements and that the patient receive the appropriate evaluation and management of treatable barriers.

A 37-year-old woman of Portuguese descent infected with both hepatitis C virus (HCV) and HIV (CD4 cell count while not taking highly active antiretroviral therapy, >400 cells/mm3) who was actively engaged in injection opioid use was admitted into a public health hospital for treatment of altered mental status related to drug use. She was from a socioeconomically depressed community that had a large percentage of injection drug users (IDUs).

The patient is of premorbid, low-average range of intellectual functioning and left school in the eighth grade. Since her teenage years, she had a number of psychiatric hospitalizations related to physical aggression and drugs, including 1 court-mandated inpatient evaluation. In addition, she had been incarcerated >8 times for crimes, including simple possession of narcotics, commercial sex work, and assault.

While incarcerated in state prison, the patient met her infectious disease physician. A rapport developed between them, and, when the patient was released to the community, she elected to follow up with this same doctor. Over the next year, the patient had several hospitalizations associated with mental status changes and abuse of benzodiazepines and over-the-counter medications. During this time, the patient was noncompliant with prescribed psychotropic medications, primarily because of weight gain.

The infectious disease physician referred this patient to the psychiatrist working with the HIV-HCV Coinfection Clinic at Lemuel Shattuck Hospital (Jamaica Plain, MA) for evaluation of the patient’s treatment readiness for therapy with IFN and ribavirin for HCV infection.

TREATMENT READINESS

Treatment readiness can be defined as the patient’s motivation to adhere to treatment. Although the patient

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may not achieve 100% adherence, open communication and willingness to try to adhere are imperative. Four identifiable barriers to establishing treatment readiness are mood and anxiety disorders, cognitive deficits, temperament disorders, and ongoing drug use. If properly addressed, these barriers can be overcome.

**MOOD AND ANXIETY DISORDERS**

The prevalence of mood and anxiety disorders in the population of substance abusers is pronounced, compared with that in the general population. In the 1980s, Rounsaville et al. [1], of Yale University (New Haven, CT), studied 533 opioid addicts receiving substance abuse treatment; 421 patients were entering treatment, and 120 were undergoing maintenance treatment with methadone. They reported that 70% of the patients had a current psychiatric diagnosis, 53% met criteria for a lifetime prevalence of major depression, and 52% had ≥2 psychiatric diagnoses independent of addiction. Bipolar disorder and schizophrenia were not represented among IDUs more than in the general population, thus disproving the idea that the population of IDUs might have an increased prevalence of all psychosocial disorders.

In a more recent study of 116 subjects, Franken and Hendricks [2] measured the prevalence of mood and anxiety disorders in a substance-dependent population. In their cohort, 51% of the population identified heroin as their drug of choice, and 11% identified injection as their route of administration. During the study, 38.8% had a current prevalence of an anxiety disorder, and 53% showed lifetime prevalence. Concerning mood disorders, the study showed a 21% current prevalence and a 49% lifetime prevalence (table 1).

Patients taking IFN therapy have a risk of developing cytokine-mediated sickness syndrome [3], which has symptoms similar to those of major depressive disorder. Abnormalities of mood, interest, appetite, libido, social withdrawal, somatization, and cognitive difficulties can be present in both illnesses. However, in the sleep laboratory, rapid eye movement and non–rapid eye movement sleep patterns will differentiate major depressive disorder from cytokine-mediated sickness syndrome. Research has not identified accurate predictors for development of cytokine-mediated sickness syndrome.

In the past, data based on small sample sizes and anecdotal reports deterred hepatologists and infectious disease physicians from treating HCV-infected patients with psychiatric disorders. In a study from 2001 of a population of veterans taking IFN, more than half of whom had preexisting psychiatric diagnoses, Ho et al. [4] found that 68% developed major adverse events that required intervention or discontinuation of treatment.

Treatment practices are changing in response to new evidence in this area. In a more recent study [5], 88 HCV-positive patients treated with IFN-α and ribavirin were divided into 4 groups: a control group, a psychiatric disorders group, a group of patients undergoing maintenance therapy with methadone, and a group of former addicts. The group with psychiatric diagnoses received more antidepressant therapy before and during treatment. However, no subject in the psychiatric disorders group had to discontinue treatment secondary to psychiatric diagnoses independent of addiction. Bipolar disorder and schizophrenia were not represented among IDUs more than in the general population. In the 1980s, Rounsaville et al. [1], of Yale University (New Haven, CT), studied 533 opioid addicts receiving substance abuse treatment; 421 patients were entering treatment, and 120 were undergoing maintenance treatment with methadone. They reported that 70% of the patients had a current psychiatric diagnosis, 53% met criteria for a lifetime prevalence of major depression, and 52% had ≥2 psychiatric diagnoses independent of addiction. Bipolar disorder and schizophrenia were not represented among IDUs more than in the general population, thus disproving the idea that the population of IDUs might have an increased prevalence of all psychological disorders.

### Table 1. Anxiety and mood disorders among a drug-dependent population (n = 116).

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Prevalence, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anxiety disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Panic disorder without agoraphobia</td>
<td>3.4</td>
</tr>
<tr>
<td>Generalized anxiety disorder</td>
<td>10.3</td>
</tr>
<tr>
<td>Panic disorder with agoraphobia</td>
<td>5.2</td>
</tr>
<tr>
<td>Agoraphobia without panic disorder</td>
<td>15.5</td>
</tr>
<tr>
<td>Social phobia</td>
<td>31.0</td>
</tr>
<tr>
<td>Simple phobia</td>
<td>32.8</td>
</tr>
<tr>
<td>Obsessive compulsive disorder</td>
<td>4.3</td>
</tr>
<tr>
<td>Any anxiety disorder</td>
<td>53.4</td>
</tr>
<tr>
<td><strong>Mood disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Dysthymia</td>
<td>17.2</td>
</tr>
<tr>
<td>Major depression</td>
<td>35.3</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>7.8</td>
</tr>
<tr>
<td>Any mood disorder</td>
<td>49.1</td>
</tr>
<tr>
<td>Any anxiety or mood disorder</td>
<td>69.8</td>
</tr>
</tbody>
</table>

**NOTE.** Anxiety and mood disorders are defined according to the Diagnostic and Statistical Manual of Mental Disorders, 3rd edition, revised (Composite International Diagnostic Interview). Reprinted with permission from [2].
spurred the use of prophylactic antidepressant therapy for many of our IFN- and ribavirin-treated patients, to prevent cytokine-mediated sickness syndrome.

COGNITIVE DEFICITS

Cognitive deficits in this population can affect the patients’ ability both to engage in treatment and to adhere to a complicated medical regimen. Evidence for HCV infection of the CNS [7] is growing; however, information about its direct effects on cognitive functioning is limited. Minimal hepatic encephalopathy can cause subclinical mental dulling. Physicians need to be aware of subtle signs as well as the more obvious confusion or abnormal psychomotor activity that suggest the presence of hepatic encephalopathy. Physicians should also have full knowledge of their patients’ current medication regimen, including potential drug-drug interactions and adverse-effect profiles, which can alter cognition and, in turn, treatment readiness.

In the population of IDUs, many HCV-positive patients are coinfected with HIV. With HIV, there is risk for minor cognitive motor disorder [8]. Minor cognitive motor disorder presents subclinically, and neurological and/or neuropsychological testing is necessary for diagnosis (table 2).

A risk for HIV-positive patients with CD4 cell counts of <200 cells/mm^3 is HIV-associated dementia. This complication of HIV is treatable but can cause patients to develop problems in terms of communicating with the provider and adhering to a treatment regimen. Awareness of the symptom complex and evaluation of the patient before treatment of HCV allows for realistic planning of treatments.

Patients with HIV-associated dementia generally exhibit frontal lobe signs associated with executive and nonexecutive system dysfunction. Nonexecutive function deals with problem solving, behavioral self-regulation, referencing past experience, and the ability to anticipate consequences. Executive function involves decision-making skills, information filtering, intellectual flexibility, and task-completion skills. In addition, there are a number of affective signs and symptoms of HIV-associated dementia, including depressed mood, mania, anxiety, and agitation.

TEMPERAMENT DISORDERS AND PERSONALITY VULNERABILITIES

The third barrier to treatment, disorders of temperament, often presents as a contentious relationship between the provider and the patient. Because a diagnosis of “personality disorder” has become a pejorative term, Treisman et al. [9] suggest the use of the descriptives “personality vulnerabilities” and “disorders of temperament.” These disorders manifest as maladaptive patterns of behavior that severely impair functioning in many areas of life. Treisman et al. [9] use the model of stability-instability and introversion-extroversion to explain how the unstable patient manifests high emotionality and unpredictability, whereas the extrovert is impulsive and seeks instant gratification. An unstable extrovert will have difficulty with compliance and may engage in risky behaviors. With a clinic load of hundreds of complicated patients, the provider’s approach must be multifaceted and include team treatment, behavioral contracts, cognitive behavioral therapy, and a psychopharmacological evaluation.

Cognitive behavioral therapy is often effective for temperament-disordered patients. It helps patients evaluate and organize their emotional reactions to environmental stimuli. The cognitive behavioral therapist helps patients recognize how their cognitive “take” is distorted and how they can change their behaviors [10].

ONGOING DRUG USE

Addiction should be viewed as a relapsing and remitting disorder with biological and volitional components. Many patients have a genetic predisposition to becoming drug addicted. In addition, social factors (e.g., community instability, peer group, and culture) weigh heavily in this equation. The major factors of addiction—that is, the agent, the environment, and the host—are commonly appreciated, as modeled after work by Vaillant [11]. Drug use itself is not the obstacle to treatment.

IDUs can be grouped into 2 broad demographic categories on the basis of age. One group is composed of younger addicts, usually <35 years old, who are committed to the lifestyle of the chase, the capture, and the high. This behavior is part of a social compact. Research by Ompad et al. [12] of young IDUs showed that, after education about the routes of disease transmission, 17% of young IDUs did not increase or decrease their behaviors 

| Table 2: Signs of minor cognitive motor disorder resulting from HIV infection of the CNS. |
| Signs |
| Cognitive/motor/behavioral dysfunctions (≥2 for 1 month) |
| Impaired attention or concentration |
| Mental slowing |
| Impaired memory |
| Slowed movements |
| Incoordination |

NOTE. Minor cognitive motor disorder is assessed by neurological examination or neuropsychological testing. Reprinted with permission from [8]. |
phenomenon to categorize the second group of IDUs, who are >35 years old. There tends to be a period when IDUs begin to slowly taper off their use of needles and pick up alcohol and pills. In many ways, this is much more problematic concerning treatment readiness for HCV-positive IDUs. Patients who abuse alcohol and benzodiazepines present with decreased mental acuity, making communication difficult.

Many opioid addicts can be alert and can function well when not in pursuit of illegal drugs. In a study by Broers et al. [14], 2 groups of patients (151 IDUs and 162 control subjects) were measured for compliance with zidovudine regimens. Those authors did not find any significant difference between the 2 groups with regard to compliance; 81.3% of IDUs and 83.2% of control subjects had good compliance, as defined by ≥80% adherence to therapy with zidovudine. The IDU cohort was further stratified to show that 66.6% of active IDUs were compliant with the medication regimen, compared with 84.8% of stable methadone users and 61.1% of unstable methadone users. This research suggests that the ability of IDUs to adhere can be confounded more by unstable housing and psychiatric illness than by drug use per se.

Cultural, social, and drug treatment issues play an enormous part in patients’ readiness for treatment and must be addressed before initiating medical treatment for HCV. Bringing HCV-positive active IDUs to treatment is difficult, as reflected in data collected from a public detoxification level III (as defined by criteria of the American Society of Addiction Medicine) facility in Jamaica Plain, Massachusetts, serving a disenfranchised inner city population of overwhelmingly black and Latino people (personal communication). In 2002, this facility had 2648 admissions, of which 61% of patients were opioid dependent; in a client survey of all admissions, only 2% of patients reported having a primary care physician. This particular center had a 30% recidivism rate and was recently closed by the state government because of budget cutbacks. Facilities hampered by budget cuts lack effective education and referral systems.

An option that can increase adherence to a treatment regimen is to treat patients with legal opioid substitution therapy (e.g., methadone or buprenorphine). Current research is under way to evaluate directly observed therapy with IFN or ribavirin for HCV-positive patients who are undergoing maintenance treatment with methadone. Unfortunately, treatment slots are limited by regulations of the US Department of Health and Human Services Substance Abuse and Mental Health Services Administration. In previous years, buprenorphine was available to treat opioid-dependent patients in inpatient settings. Buprenorphine works well by means of partial opioid agonist-antagonist properties. At low doses, it prevents withdrawal by acting as an agonist, and, at high doses, there is a ceiling effect on respiratory depression. In early 2003, buprenorphine was approved by the US Food and Drug Administration for outpatient detoxification and maintenance use and may be prescribed by physicians to outpatients in an office setting, rather than being restricted to federally regulated clinics. A formulation containing buprenorphine and naloxone, a pure opioid antagonist that precipitates withdrawal if the medication is crushed and injected, is available as well. Buprenorphine offers patients more flexibility and circumvents the methadone clinic culture, which often encourages relapse by virtue of proximity to agent and environment.

Drug use is not an obstacle to treatment, but risky drug use—for example, needle sharing—should be considered a barrier to treatment. Providing access to clean needles is an essential tool for prevention of the spread of HCV. Taylor et al. [15] surveyed 104 physicians at an American Society of Addiction Medicine conference regarding prescription of syringes. Even though physicians may legally prescribe syringes in 48 states, many are still reluctant to do so, with psychiatrists being the most disinclined group. Only 2 respondents had ever prescribed syringes to an IDU knowing that this equipment would be used for injecting illicit substances. Physicians need to reevaluate the long-term benefit of needle prescription for IDUs.

**APPROCING THE BARRIERS**

Physicians are able to elicit optimal results by being aware of and addressing known barriers to treatment readiness. The approach to assessing the treatment readiness of an HCV-positive IDU must begin with a psychiatric evaluation. Initial interventions, such as neuropsychological testing, are essential in terms of diagnosing dementia and cognitive deficits.

Rapport is a connection between medical provider and patient; it is best established by creating a paradigm of accessibility, interest, and follow-up. A team approach and exquisite patience are cardinal parts of a strategy to actualize an educated and involved patient. Psychopharmacology and opioid substitution therapy are important treatment options. Nonpharmacological management—including cognitive behavioral therapy, supportive therapy, outreach programs [16], needle exchange, prescription of syringes [17], behavioral contracts, use of the courts for stipulation of treatment, and residential programs—addresses many of the issues that impede treatment (table 3).

**CASE CONCLUSION**

The patient described above was evaluated and followed by an addiction psychiatrist in the HIV/HCV Coinfection Clinic at Lemuel Shattuck Hospital. Neuropsychological testing was done, and executive system dysfunction was identified; placement in supervised housing was recommended. An outreach social worker assisted with securing an appropriate housing assignment and application to a methadone maintenance program. After 9 months of preparation—including adjustments in

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psychotropic medications that facilitated the patient’s compliance, a behavioral contract requiring proven attendance at weekly appointments, supportive therapy, and a month of residential treatment during a drug relapse—the clinicians initiated therapy with IFN and ribavirin. Despite the patient’s limited virological response, she completed 32 weeks of treatment. The successful treatment of this patient depended on a full complement of medical and social supports. Considering the variability of social and medical problems of the HCV-positive IDU population, clinicians should apply similar approach to assess the level of treatment readiness of their patients.

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